

Amendment to the specification:

Insert the paper copy of the Sequence Listing filed herewith following the Drawings.

Please amend the paragraph beginning at page 9, which starts with "*DNA sequence*", as follows:

*DNA sequence (Factor X sequence shown in gray):*

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GAC TCT AAG AAA GAC ATT TCG AAT GTT AAA AGT GAT TTA CTT TGC
GCA TAC ACT ATA ACT CCT ATC GAA GGT CGT ACG CCT GCT CAA AAT
AAT AAA GTA AAT CAT AAA TTA TTG GGA AAT CTA TTT ATT TCG GGA
GAA TCT CAA CAG AAC TTA AAT AAC AAG ATT ATT CTA GAA AAG GAT
ACC GTA ACT TTC CAG GAA ATT GAC TTT AAA ATC AGA AAA TAC CTT
ATG GAT AAT TAT AAA ATT TAT GAC GCT ACT TCT CCT TAT GTA AGC
GGC AGA ATC GAA ATT GGC ACA AAA GAT GGA AAA CAT GAG CAA ATA
GAC TTA TTT GAC TCA CCA AAT GAA GGG ACT AGA TCA GAT ATT TTT
GCA AAA TAT AAA GAT AAT AGA ATT ATC AAT ATG AAG AAC TTT AGT
CAT TTC GAT ATT TAT CTT GAA AAA TAA (SEQ ID NO:5)
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Please amend the paragraph beginning at page 9, which starts with "*Protein sequence*", as follows:

*Protein Sequence:*

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DSKKDISNVKSDLLCAYTITPIEGRTPAQNNKVNHLKLLGN
LFISGESQQNLNNKIILEKDTVTFQEIDFKIRKYLMDNYKIYDA
TSPYVSGRIEIGTKDGKHEQIDLFDSPNEGTRSDIFAKYKDNRII
NMKNFSHFDIYLEK Stop (SEQ ID NO:6)
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Please amend the Table 1 beginning at page 12, as follows:

Table 1: Primers used for amplification of the SPEC gene and introduction of mutations or truncations

|                   |  |  |
|-------------------|--|--|
| SPEC – N-terminal | CGGGATCCGACTCTCAAGAAAGACA (SEQ ID NO:7)              |  |
| SPEC – C-terminal | CTGAATTCTTATTTTCAAGAT (SEQ ID NO:8)                  |  |
| SPEC- Y15A        | GATTTACTTTGTGCATACAC (SEQ ID NO:9)                   | GTGTATGCACAAAGTAAATC (SEQ ID NO:15)            |
| SPEC- N79C        | ATATTCTTTGTTCTCACA (SEQ ID NO:10)                    | TATAAGAAACAAGAGTGT (SEQ ID NO:16)              |
| SPEC- Y15C        | GATTTACTTTGTGCATACAC (SEQ ID NO:11)                  | GTGTATGCACAAAGTAAATC (SEQ ID NO:17)            |
| SPEC- R181Q       | GAAGGGACTCAATCAGATATTTTGC<br>(SEQ ID NO:12)          | GACAAAATATCTGATTGAGTCCCTTC (SEQ ID NO:18)      |
| SPEC-(-20-90)     | ATCGAAGGTCGTACGCCTGCTCAAAATAATAAAG<br>(SEQ ID NO:13) | ACGACCTTCGATAGGAGTTATAGTGTAT<br>(SEQ ID NO:19) |
| SPEC- C27S        | GATTATAAAGATTCCAGGGTAA (SEQ ID NO:14)                | TTACCCTGGAATCTTTATAATC (SEQ ID NO:20)          |

Please amend the paragraph beginning at page 17, line 1, as follows:

Primary DNA sequences of the wild-type and the mutant form of SPE-C are detailed below:

*SPE-C wild type (from GenBank)*

**Streptococcus pyogenes pyrogenic exotoxin C gene, 5' end cds**

GACTCTAAGA AAGACATTTT GAATGTTAAA AGTGATTTAC TTTATGCATA CACTATAACT  
CCTTATGATT ATAAAGATTG CAGGGTAAAT TTTTCAACGA CACACACATT AAACATTGAT  
ACTCAAAAAT ATAGAGGGAA AGACTATTAT ATTAGTTCGG AAATGTCCTA TGAGGCCTCT  
CAAAAATTTA AACGAGATGA TCATGTAGAT GTTTTGGAT TATTTTATAT TCTTAATTCT  
CACACCGGTG AGTACATCTA TGGAGGAATT ACGCCTGCTC AAAATAATAA AGTAAATCAT  
AAATTATTGG GAAATCTATT TATTTCCGGA GAATCTCAAC AGAACTTAAA TAACAAGATT  
ATTCTAGAAA AGGATATCGT AACTTTCCAG GAAATTGACT TTTAAATCAG AAAATACCTT  
ATGGATAATT ATAAAATTTA TGACGCTACT TCTCCTTATG TAAGCGGCAG AATCGAAATT  
GGCACAAAAG ATGGGAAACA TGAGCAAATA GACTTATTTG ACTACCAAA TGAAGGGACT  
AGATCAGATA TTTTTCGAAA ATATAAAGAT AATAGAATTA TCAATATGAA GAACTTTAGT  
CATTTGATA TTTATCTTGA A (SEQ ID NO:1)

**Protein Sequence – wild type**

DSKKDISNVK SDLLYAYTIT PYDYKDCRVN FSTHTLNIID TQKYRGKDYY ISSEMSYEAS  
QKFKRDDHVD VFGLFYILNS HTGEYIYGGI TPAQNNKVNH KLLGNLFISG ESQQLNNKI  
ILEKDIVTFQ EIDFKIRKYL MDNYKIYDAT SPYVSGRIEI GTKDGKHEQI DLFDSPNEG  
RSDIFAKYKD NRIINMKNFS HFDIYLE (SEQ ID NO:2)

**SPEC- Y15A.C27S.N79C.R181Q**

GACTCTAAGA AAGACATTTC GAATGTTAAA AGTGATTACT TATGCATA CACTATAACT  
GATTTACT TTGTGCATA CAG  
C27S  
CCTTATGATT ATAAAGATTC CAGGGTAAAT TTTTCAACGAC ACACACATT AAACATTGAT  
GATT ATAAAGATTTC CAGGGTAA  
ACTCAAAAAT ATAGAGGGAA AGACTATTAT ATTAGTTCCGA AATGTCTTA TGAGGCCTCT  
N79C  
CAAAAATTTA AACGAGATGA TCATGTAGAT GTTTTGGATT ATTTTATAT TCTTAAATCT  
ATAT TCTTTGTCT  
CACACCGGTG AGTACATCTA TGGAGGAATT ACGCCTGCTCA AAATAATAA AGTAAATCAT  
CA  
AAATTATTGG GAAATCTATT TATTTCCGGA GAATCTCAACA GAACTTAAA TAACAAAATT  
ATTCTAGAAA AAGATATCGT AACTTTCCAG GAAATTGACT TTAAAATCAG AAAATACCTT  
ATGGATAATT ATAAAATTTA TGACGCTACT TCTCCTTATG TAAGCGGCAG AATCGAAATT  
GGCACAAAAG ATGGGAAACA TGAGCAAATA GACTTATTTG ACTCACCAA TGAAGGGACT  
GAAGGGACT  
R181Q  
AGATCAGATA TTTTTCGAAA ATATAAAGAT AATAGAATTA TCAATATGAA GAACTTTAGT  
CAATCAGATA TTTTTCG  
CATTTGATA TTTATCTTGAA (SEQ ID NO:3)

**Protein Sequence (combined mutants)**

DSKKDISNVK SDLLAAYTIT PYDYKDSRVN FSTHTLNID TQKYRGKDYY ISSEMSYEAS  
QKFKRDDHVD VFGLFYILCS HTGEYIYGGI TPAQNNKVNH KLLGNLFISG ESQQLNNKI  
ILEKDIVTFQ EIDFKIRKYL MDNYKIYDAT SPYVSGRIEI GTKDGGKHEQI DLFDSPPNEG  
QSDIFAKYKD NRIINMKNFS HFDIYLE (SEQ ID NO:4)

Please amend the paragraph beginning at page 20, which starts with "The primary nucleotide", as follows:

The primary nucleotide sequence of truncated version of SPE-C is detailed below:

*DNA sequence (Factor X sequence shown in gray):*

GAC TCT AAG AAA GAC ATT TCG AAT GTT AAA AGT GAT TTA CTT TGC GCA TAC ACT  
ATA ACT CCT ATC GAA GGT GGT ACG CCT GCT CAA AAT AAT AAA GTA AAT CAT AAA  
TTA TTG GGA AAT CTA TTT ATT TCG GGA GAA TCT CAA CAG AAC TTA AAT AAC AAG  
ATT ATT CTA GAA AAG GAT ACC GTA ACT TTC CAG GAA ATT GAC TTT AAA ATC AGA  
AAA TAC CTT ATG GAT AAT TAT AAA ATT TAT GAC GCT ACT TCT CCT TAT GTA AGC  
GGC AGA ATC GAA ATT GGC ACA AAA GAT GGA AAA CAT GAG CAA ATA GAC TTA TTT

GAC TCA CCA AAT GAA GGG ACT AGA TCA GAT ATT TTT GCA AAA TAT AAA GAT AAT  
AGA ATT ATC AAT ATG AAG AAC TTT AGT CAT TTC GAT ATT TAT CTT GAA AAA TAA  
(SEQ ID NO:5)

*Protein Sequence*

D S K K D I S N V K S D L L C A Y T I T P **I E G R** T P A Q N N K V  
N H K L L G N L F I S G E S Q Q N L N N K I I L E K D T V T F Q E  
I D F K I R K Y L M D N Y K I Y D A T S P Y V S G R I E I G T K D  
G K H E Q I D L F D S P N E G T R S D I F A K Y K D N R I I N M K  
N F S H F D I Y L E K Stop (SEQ ID NO:6)

Please amend the paragraph beginning at page 21, which starts with "Synthetic peptide", as follows:

Synthetic peptide containing a C-terminal cysteine residue and SPEC-Y15A.C27S.N79C are mixed together and incubated at room temperature for 1 hour at a molar ratio of 1:2 in a alkaline buffer containing 1  $\mu\text{M}$   $\text{Cu}^{2+}$ . The copper acts as a redox catalyst. In the example below, a synthetic peptide of the pigeon cytochrome C (PCC) is provided, but this method will work for other peptides also so long as a free sulphur atom is present in the peptide.

| SPEC-<br>Y15A.C27S.N79C.R181<br><br>Q<br>(MW 26,500)<br>10 mg/ml<br>(380 $\mu\text{M}$ ) | PCC peptide<br>(RADLIAYLKQATKC)<br>(SEQ ID NO:21)<br>(MW 1400) 10 mg/ml<br>(700 $\mu\text{M}$ ) | Buffer   |
|--|---|--|
| 100 $\mu\text{l}$  | 10 $\mu\text{l}$  | 200mM Tris pH8.0, 1 $\mu\text{M}$<br><br>$\text{CuSO}_4$ |

Please amend the paragraph beginning at page 22, which starts with "The 5C.C7 transgenic", as follows:

The 5C.C7 transgenic mouse was originally constructed by Berg et al.<sup>17</sup>. This mouse is transgenic for a TcR specific for the pigeon cytochrome C (PCC) peptide presented by mouse I-A<sup>d</sup>. Greater than 80% of mature T cells from 5C.C7 mice express the transgenic TcR and respond to synthetic PCC peptide RADLIAYLKQATK (SEQ ID NO:22) in vitro. This mouse

provides an excellent means to test PCC specific T cell responses both in vitro and in vivo as well as conduct adoptive transfer experiments. Adoptive transfer is a powerful method that allows the introduction of PCC reactive T cells into non-transgenic mice to study responses at varying T cell precursor frequencies.